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PATENT COOPERATION TREATY

From the INTERNATIONAL BUREAU

PCT

NOTIFICATION OF ELECTION

(PCT Rule 61.2)

To:

Commissioner
US Department of Commerce
United States Patent and Trademark
Office, PCT
2011 South Clark Place Room
CP2/5C24
Arlington, VA 22202
ETATS-UNIS D'AMERIQUE

in its capacity as elected Office

Date of mailing (day/month/year) 04 May 2001 (04.05.01)	
International application No. PCT/GB00/03061	**Applicant's or agent's file reference** 331
International filing date (day/month/year) 14 August 2000 (14.08.00)	**Priority date** (day/month/year) 13 August 1999 (13.08.99)
Applicant CROCKER, Peter, John	

1. The designated Office is hereby notified of its election made:

[X] in the demand filed with the International Preliminary Examining Authority on:

06 March 2001 (06.03.01)

[ ] in a notice effecting later election filed with the International Bureau on:

2. The election [X] was

[ ] was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO
34, chemin des Colombettes
1211 Geneva 20, Switzerland

Facsimile No.: (41-22) 740.14.35

Authorized officer

Olivia TEFY

Telephone No.: (41-22) 338.83.38

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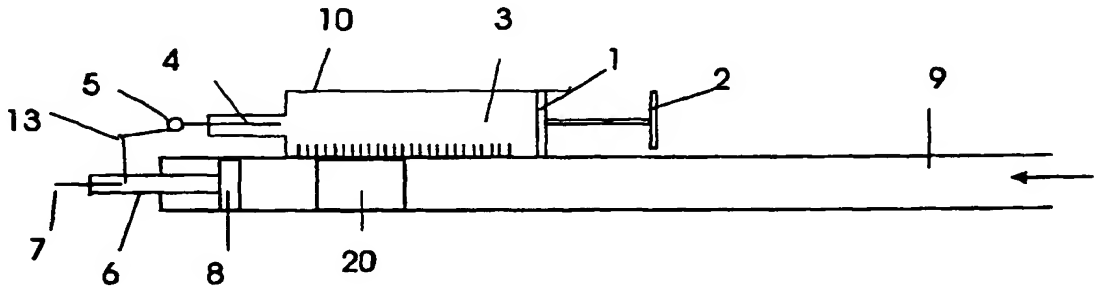
Published:
— *With international search report.*

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: INJECTION MEANS



(57) Abstract: Injection apparatus has the needle of low mass struck by a fast moving block causing a needle to be accelerated very rapidly and easily to high speeds to reduce the pain of penetration and then, when the needle has penetrated the skin the substance is injected.

WO 01/12252 A1

Injection Means

This invention relates to improvements in devices for delivery of substances such as drugs, vaccines, fluorescent or magnetic material, and dyes into a surface, such as the skin of a human being, animal or other organic matter. The substance may be a solution, particulate fluid, or a paste, for example.

Numerous such apparatus have been proposed in the past. A simple hypodermic syringe is the most well known although other mechanical arrangements, such as an auto-injector which are manually operated are well known.

Also mechanically operated apparatus have been proposed to facilitate injections and this enables higher speed of injections to be achieved which can reduce the pain of the injection and consequent bruising, bleeding etc.

US Patent 5681283 discloses the use of a system in which needles are injected into the skin using elastic bands at a high velocity with the intention of making the injection "painless" and US Patent 5564436 discloses a pneumatically operated automatic rotating cassette with a plurality of stylets so that the higher velocity can reduce the pain of the injection.

We have now devised an improved apparatus and method for injecting substances into a surface which facilitates the use of higher speeds.

According to the invention there is provided apparatus for injecting a substance into a surface which apparatus comprises a needle, a container for the substance to be injected, a means for applying the substance from the container to the tip of the needle, a means for driving the needle to penetrate the surface and deliver the substance thereto which means comprises a block slidably mounted in a conduit

which block is accelerated by a controlled force to strike the needle assembly thereby inducing an acceleration of the needle to drive it into the surface.

Preferably there is a connection between the needle and the container which has sufficient flexibility to allow the needle to penetrate the skin without the connection being broken.

In existing hypodermic syringes and other apparatus the needle is directly attached to the container for the substance being injected and the needle and container move as one unit so the needle penetrates the surface.

However when a higher velocity of injection is used sufficient force must be applied to accelerate the needle plus container plus substance being injected to the desired velocity and to stop them, either by the frictional resistance to the injection by the surface or by a stop mechanism and the greater the mass, the greater the forces and energy required and the more likelihood of pain, bruising, bleeding etc. when the needle penetrates. In addition the greater the mass the more robust and heavy the driving means must be and the greater the noise in operation, greater wear etc.

The present invention minimises the driven mass and so reduces or overcomes these problems.

If the mass of the fluid to be injected is sufficiently low the reservoir for the fluid can be incorporated with the needle so that the needle and reservoir are accelerated as one unit, the volume of fluid should be less than 1ml e.g. mass of fluid should be less than 1 grm.

Preferably the needle holder mass (together with fluid reservoir if included) i.e. the mass of the needle and associated moving parts is 0.01 to 5.0grm, more preferably 0.1 to 3grms and most preferably 0.2 to 0.6grm., with a typical mass being about

0.6grms., this also means that the needle and other connected components have less kinetic energy and this reduces the risk of bruising etc. This is different to other techniques of injection, such as the injection of animals with tranquillising darts, when the needle penetrates the surface and forms part of, or is rigidly connected directly to a chamber containing the substance to be injected.

Preferably the mass of the block is from 0.8 to 3 times the needle holder mass and more preferably from one to twice the mass.

The present invention enables very high acceleration of the needle to be attained and the acceleration of the needle is preferably 1 to 20,000g.

Under these conditions of high acceleration and/or high velocity it is important that the needle moves very straight along its axis and any lateral or transaxial movement or flex is kept to a minimum. In one embodiment of this invention the block is made to move very straight along its axis and to strike the needle assembly squarely and centrally. Also the needle assembly preferably includes a guide to restrict lateral or transaxial movement and this also minimises flex.

The needle driving means may include one or more of a leaf spring and stop arrangement, or a bistable spring or diaphragm arrangement. The needle driving means may include a mechanically hydraulic, pneumatic or electromechanically driven drive mechanism.

A preferred driving means is pneumatically operated and comprises a block slidably mounted in a conduit so that application of a pneumatic force at one end of the conduit generates a pulse of gas e.g. air which will propel the block at speed down the conduit, so that it will strike a end piece, which is connected to the end of the needle. Preferably the block can be returned to its original position by reduction of

pressure in the conduit. In this way one or more pulsed impulses can be applied to the end piece with the block being withdrawn back down the conduit between pulses.

Preferably the block is positioned in contact with the source which generates the pulse of air so that the end of the block acts as a seal and is held in position with air pressure built up behind the block. When a release mechanism is operated the block is free to move and is propelled by the air pressure down the conduit. A preferred seal is for the end of the block to have a tapered shape and to fit into a corresponding shape at the end of tube connected to the pneumatic source so that the end of the block forms a tight seal. The end of the block acts as a plug valve and can form a tight fit and is held in position by frictional forces. To operate, the block is given a small push or nudge to overcome the frictional forces, whereupon the block moves down the conduit. The device can be primed ready for use with the block in place and air pressure built up behind the block ready for release.

The end piece which is struck can be the end of the needle suitably reinforced if need be, or it can be an end piece or the like attached to or forming part of the needle. The end piece will normally have a flat end which is struck for ease of operation although this is not essential

Suitable means for applying the pneumatic force include hand held bellows, pre-compressed gas, a piston with a spring return or a motorised means. The bellows can, for example be in the form of a sealed rubber chamber connected to the conduit. Another means of operating is by means of a pen injector which can be conveniently carried and used as required.

There can be a source of compressed gas which generates a pulse of gas and this compressed gas can be a gas such as carbon dioxide or air etc. The pneumatic force can also be generated by the generation of a gas by the evaporation of a liquid such as

water or an organic liquid e.g. by an electrical heater so the gas formed propels the block down the conduit.

In another embodiment there is a reduction of pressure in the conduit below the block in the direction the block moves i.e. so that a partial vacuum is formed and this reduction in pressure propels the block. The block is then "sucked" down the conduit.

This method using a reduction in pressure can be used on its own or in conjunction with the application of pneumatic force as described above, either sequentially or simultaneously.

In a preferred embodiment of the invention there is provided a means whereby the needle is driven into the skin in steps by contacting the skin with the needle, applying a blow to the needle e.g. as described above so that the needle penetrates a controlled distance into the skin and then optionally applying another blow or blows to the needle to drive the needle in to the desired depth.

For example the needle can be driven into the skin until it is in contact with bone and then a blow is applied to the needle to drive it into the bone e.g. to inject into the bone marrow. The mass of the shuttle and needle holder should be sufficient to drive the needle through the bone to the required depth.

If a plurality of blows are required this can be carried out as described above and/or there can a two or more blocks slidably mounted within the conduit so that a plurality of blows impact on the end piece.

Alternatively the needle and block can be slidably connected together and spaced apart so that they are propelled down the conduit together and, when the needle enters the skin and stops, the block continues and strikes the end of the needle so that there

is a double hit i.e. when the needle strikes and enters the skin and then when the block strikes the end of the needle and drives it further in.

In another embodiment, a valve and port arrangement, known to those skilled in pneumatics, used with compressed gas drives the block towards the needle assembly. When the block reaches the end of its travel, the valves exhaust the forward driving pressure and apply pressure in the reverse direction to the block. The reciprocating cycle is then repeated as often as required.

In another embodiment part of the momentum of the moving block can be transferred to the syringe plunger to induce pressure which injects a quantity of the substance to be injected into the skin.

If a rapid series of injections are required e.g. in which the needle penetrates only a small distance into the skin, a motorised means can be used to generate the pulse of air and subsequent reversal of pressure.

In one embodiment of the invention the substance to be injected is contained in a reservoir fluidically connected to the needle and there are means to accelerate the needle independently without accelerating the reservoir. This means that there is less mass to be accelerated so it is easier to accelerate and to stop the needle.

The feed of the substance to the needle can be discontinuous and synchronised to the time when the needle is beneath the skin so that a series of small volumes of the substance can be injected into the patient.

The needle can be separate and adjacent to a syringe containing the substance to be delivered with one end of the needle flexibly connected to the end of the syringe by for example a flexible tube or by a coiled length of the needle so that rapid movement of the needle is not is not significantly inhibited by connection to the syringe. The

needle is driven by the driving means until it has penetrated to the required depth and then the syringe is operated to inject the substance contained in the syringe through the needle into the surface.

In another embodiment a syringe has a piston operating in the normal way with the needle projecting through the end of the syringe and the needle having an extension projecting through the piston so the end of the extension can be struck by a driving means to drive the needle into a surface, there being a connection means between the syringe and the needle whereby the substance in the syringe can pass through the needle from the syringe as the piston is depressed. In use the needle is placed against the surface and the end of the extension is struck as referred to above to drive the needle into the surface and then, when it has been driven into the required depth, the piston is depressed to inject the substance in the syringe into the surface.

Preferably the needle is driven into the skin of the user by applying one or more impacts to the end of the needle to drive the needle into the skin to the desired depth and then the substance to be delivered is applied through the needle.

Optionally there can be a needle guide which can fit around the needle to assist in the location and positioning of the needle and keeps the needle exactly on line during the injection and reduces any risk of the needle bending. In addition the guide can help guard against needle stick injury when the needle is withdrawn and can serve as a depth control.

It is a feature of the invention that the mass which has to be accelerated to high velocities is much less than in other techniques which enables low energy to be used to propel the needle and makes it much easier to stop. It enables very high accelerations e.g. 1 to 20,000 g to be easily achieved by simple means. For example the pneumatic pressure required can be obtained by blowing down the conduit.

It has been found that the needles used can be blunter and it has been found that, for at least some applications, a blunter needle i.e. one which has a rounded or conical tip and which has no, or less sharp, cutting surfaces compared to a typical hypodermic needle or lancet can be used and this structure can cause less cutting of capillaries and bleeding. This is thought to be due to the blunter needle, when driven at the speeds of the present invention, forces the components of the skin such as capillaries, cells etc. apart rather than cutting them as would be done with sharper needles. This reduces the risk and incidence of bruising and the possible formation of fibroids and the like. For some people such as haemophiliacs this is a great advantage.

This advantage was surprising and contrary to what would otherwise be thought as it is difficult, painful and causes tissue damage to penetrate skin with a blunt needle unless the skin has been pre-cut.

Preferably the needle is hollow with at least one aperture connecting to core directly adjacent to the tip to allow injections to be made at a depth optionally of less than 1mm below the skin surface. The needle can have a substantially non-cutting tip with substantially no sharpened edges or blades with smooth, tapered, radiused or bevelled edges or surfaces.

Alternatively the needle can be conical or with a radiused point and one or more slots are present which connect the core to the exterior to allow, in use, delivery of the substance below skin surface and in which, when the needle is entering the skin, the one or more slots are substantially closed to prevent entry of external material or tissue into the core and when fluidic pressure is applied from the core to the exterior dimensions of the one or more slots increases to allow greater flow of fluidic substance.

The one or more slots can be linear and parallel to the needle axis, inclined at an angle to the axis, spiral in form or are arranged to define a moveable flap which

closes like a valve when external pressure is applied to the needle and opens like a valve when internal pressure is applied.

The present invention is particularly useful for use with high speed injection methods for example when the needle has a velocity of 1 metre per second to 100 metres per second in order to penetrate the skin and deliver the substance thereto.

Preferably the driving means drives the needle at a velocity of at 5 to 50 metres per sec, more preferably 6 to 35 metres per sec., or 10 to 20 metres per sec. e.g. 15 metres per sec.

For persons who have to have frequent injections such as diabetics, who need to inject insulin on a regular basis, the reduction of bruising, bleeding etc. is also a great advantage and the present invention is particularly applicable for use with such people.

After injection the needle can then be withdrawn from the surface and it has been found that, in at least some applications, a relatively slow withdrawal of the needle can reduce the risk of bruising to the skin.

In other applications, needle withdrawal is improved by a rapid reverse acceleration of the needle, and this can be achieved by release of a compressed spring or reverse action of the moving block for example.

There can be a connection between the needle and the block so that as the block is withdrawn the needle is withdrawn from the surface into which it was injected. This feature is particularly useful in applications such as injecting through a finger nail when, with conventional syringes the needle can be jammed in the nail and can be difficult to remove e.g. pliers have to be used to pull the needle out.

As well as for use in injecting fluids the apparatus of the present invention can also be used to aspirate.

The invention is illustrated by example in the following non limiting examples.

Example

A tube and pneumatic drive was used to accelerate a block at 0.4g to a velocity of 5 – 15 metres per sec. To strike a radius tip 28 gauge needle assembly weighing 0.2g adjacent to the skin. The needle contained a lateral hole adjacent to the tip and was driven 10mm into the skin of the arm with no pain, was able to deliver a small quantity of sterile saline to the skin and left no blood or bruising on withdrawal.

For comparison an injection device was tested which fired a 29 gauge bevel tip hypodermic needle at 4 metres per sec. into the skin of the arm to a depth of 11mm. There was significant pain, some bleeding after withdrawal of the needle and bruising developed around the penetration site taking 5 days to disappear.

The invention is described in the accompanying drawings in which

Fig. 1 is one embodiment of the invention and
Fig. 2 is another embodiment of the invention

Referring to Figure 1 a syringe (10) has a piston (1) mounted within it which can be depressed by handle (2). There is an outlet (4) from the syringe so that, when piston (1) is depressed, a substance in the body of the syringe (3) is forced out through the outlet (4). Attached to the outlet by a Luer connector (5) is one end of needle (13). The needle (13) is flexible and fixed to a holder (6) the needle can be a zig-zag shape or it can be coiled as shown in figs. 1a and 1b. Attached to holder (6) is a striker plate (8) which is the end piece to needle (13) and is slidably mounted within conduit (9),

there is block (20) positioned in the conduit. The end A of the conduit (9) is connected to pneumatic pump or the like so that air under pressure can enter the conduit and propel the block (20) down the conduit to strike plate (8). Reversal of the direction of the air in the conduit will cause the block (20) to be sucked back to the end of the conduit.

In use the substance to be injected is placed in the syringe (10) and the one or more blocks (20) are at the end of conduit (9) remote from the end of the needle (7). The end of the needle (7) is placed against the surface to be injected and a pulse of high pressure air is sent down conduit (9) so as to propel the one or more block (20), at the required high speed i.e. above 1 metre per sec, down conduit (9) to strike plate (8). The needle is then driven into the surface and an impact made on the plate (8) and the needle penetrates the surface. When the needle has penetrated the surface the piston (1) in the syringe (10) is depressed and the substance in the syringe is injected into the surface.

Referring to Figure 2 a syringe (24) has a needle (27) attached to one end and the needle has one or more openings near the tip (27) outside the syringe end seal (31) and the needle has further openings along shaft (23) lying inside the syringe end seal whereby a substance in the syringe can enter the needle. An extension (28) to the needle (27) passes slidably and sealably through the piston (25) and terminates in a striker plate (29). The striker plate is positioned in conduit (30) down which blocks can be propelled pneumatically to strike plate (29).

In use the syringe is filled with the substance to be injected and the needle (27) is placed against the surface, a block or blocks are propelled down conduit (30) in a similar way to that described for Figure 1 and striker plate (29) and so drive the needle into the surface. When the needle has penetrated the surface to the required depth the piston (25) is depressed and the substance injected into the surface.

It will be appreciated that all of the embodiments of the present invention can be arranged to deliver many different substances into skin. The substance may be a traditional tattoo dye, a temporary dye, a drug, a gene therapy substance, a particulate substance, for example.

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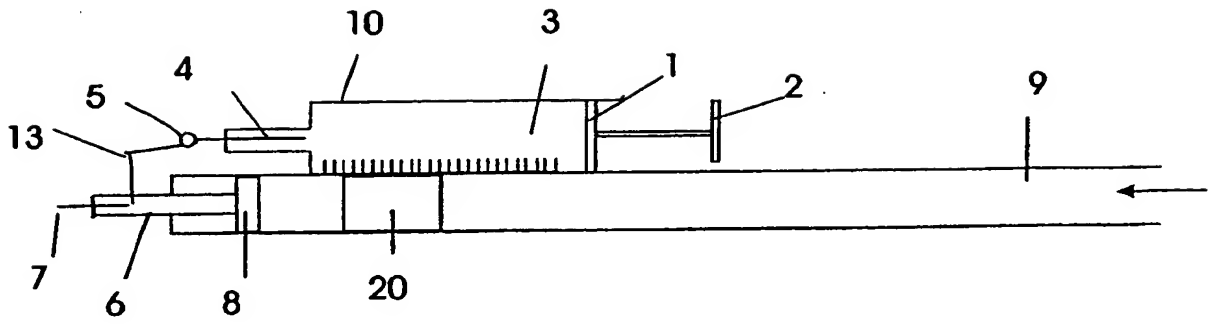

Fig. 1

Fig. 1a

Fig. 1b

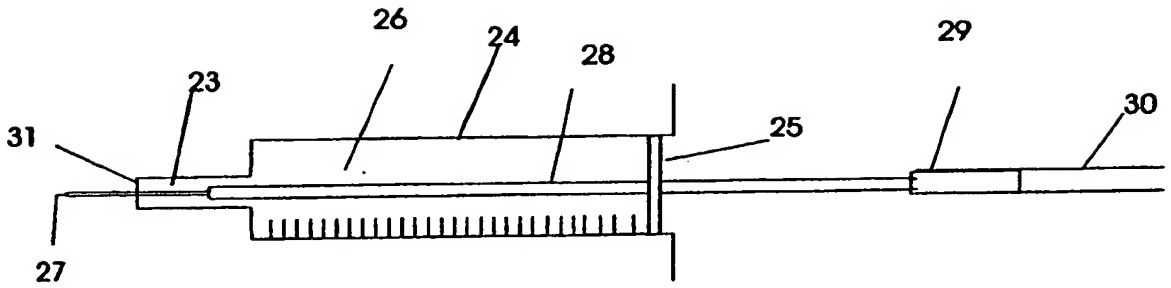

Fig. 2

INTERNATIONAL SEARCH REPORT

Intern Application No
PCT/GB 00/03061

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 A61M5/20 A61M5/42 A61M5/46 A61M5/32

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 A61M

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P,X	WO 00 09184 A (IMPRINT PHARM LTD ;CROCKER PETER JOHN (GB)) 24 February 2000 (2000-02-24) the whole document	1-9, 11-14, 17-32, 36,37,40
X	FR 1 215 970 A (P. MUSSARD) 21 April 1960 (1960-04-21) the whole document	1,11,17, 18,36
X	CH 328 609 A (DUNMIRE RUSSELL P) 15 March 1958 (1958-03-15) page 5, line 81 -page 7, line 91; figures 7-11	1,19,20, 36

-/--

[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

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"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
13 October 2000	30/10/2000

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL – 2280 HV Rijswijk Tel. (+31–70) 340–2040, Tx. 31 651 epo nl, Fax: (+31–70) 340–3016	Jameson, P

Form PCT/ISA/210 (second sheet) (July 1992)

INTERNATIONAL SEARCH REPORT

Intern[illegible] Application No
PCT/GB 00/03061

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication,where appropriate, of the relevant passages	Relevant to claim No.
X	WO 92 20388 A (MEDIMECH INT LTD) 26 November 1992 (1992-11-26) abstract; figure 1 page 7, line 4 - line 33	1,19,20, 36
A	DE 34 05 671 A (SANDOZ AG) 22 August 1985 (1985-08-22) page 18, line 22 - line 29; figures 1-4	1,25-27
A	WO 95 29720 A (PA CONSULTING SERVICES ;REVELL WILLIAM JAMES (GB)) 9 November 1995 (1995-11-09) abstract; figure 1	1

Form PCT/ISA/210 (continuation of second sheet) (July 1992)

INTERNATIONAL SEARCH REPORT

...ormation on patent family members

Intern... ...pplication No
PCT/GB 00/03061

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 0009184 A	24-02-2000	AU 5431799 A	06-03-2000
FR 1215970 A	21-04-1960	NONE	
CH 328609 A	15-03-1958	NONE	
WO 9220388 A	26-11-1992	AU 1926792 A CA 2102920 A EP 0584207 A	30-12-1992 14-11-1992 02-03-1994
DE 3405671 A	22-08-1985	NONE	
WO 9529720 A	09-11-1995	AU 2313495 A	29-11-1995

PATENT COOPERATION TREATY

From the INTERNATIONAL SEARCHING AUTHORITY

PCT

NOTIFICATION OF TRANSMITTAL OF THE INTERNATIONAL SEARCH REPORT OR THE DECLARATION

(PCT Rule 44.1)

To:
COHEN, Alan Nicol
2 Grove Place
Tatsfield near Westerham
Kent TN16 2BB
UNITED KINGDOM

Date of mailing *(day/month/year)* 30/10/2000	
Applicant's or agent's file reference 331	**FOR FURTHER ACTION** See paragraphs 1 and 4 below
International application No. PCT/GB 00/ 03061	International filing date *(day/month/year)* 14/08/2000
Applicant IMPRINT PHARMACEUTICALS LIMITED	

1. [X] The applicant is hereby notified that the International Search Report has been established and is transmitted herewith.

Filing of amendments and statement under Article 19:
The applicant is entitled, if he so wishes, to amend the claims of the International Application (see Rule 46):

When? The time limit for filing such amendments is normally 2 months from the date of transmittal of the International Search Report; however, for more details, see the notes on the accompanying sheet.

Where? Directly to the International Bureau of WIPO
34, chemin des Colombettes
1211 Geneva 20, Switzerland
Fascimile No.: (41-22) 740.14.35

For more detailed instructions, see the notes on the accompanying sheet.

2. [ ] The applicant is hereby notified that no International Search Report will be established and that the declaration under Article 17(2)(a) to that effect is transmitted herewith.

3. [ ] **With regard to the protest** against payment of (an) additional fee(s) under Rule 40.2, the applicant is notified that:

[ ] the protest together with the decision thereon has been transmitted to the International Bureau together with the applicant's request to forward the texts of both the protest and the decision thereon to the designated Offices.

[ ] no decision has been made yet on the protest; the applicant will be notified as soon as a decision is made.

4. **Further action(s):** The applicant is reminded of the following:

Shortly after **18 months** from the priority date, the international application will be published by the International Bureau. If the applicant wishes to avoid or postpone publication, a notice of withdrawal of the international application, or of the priority claim, must reach the International Bureau as provided in Rules 90*bis*.1 and 90*bis*.3, respectively, before the completion of the technical preparations for international publication.

Within **19 months** from the priority date, a demand for international preliminary examination must be filed if the applicant wishes to postpone the entry into the national phase until 30 months from the priority date (in some Offices even later).

Within **20 months** from the priority date, the applicant must perform the prescribed acts for entry into the national phase before all designated Offices which have not been elected in the demand or in a later election within 19 months from the priority date or could not be elected because they are not bound by Chapter II.

Name and mailing address of the International Searching Authority European Patent Office, P.B. 5818 Patentlaan 2 NL-2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Authorized officer Raoul Emme

Form PCT/ISA/220 (July 1998)

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference	FOR FURTHER ACTION	see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.
331		
International application No.	International filing date *(day/month/year)*	(Earliest) Priority Date *(day/month/year)*
PCT/GB 00/03061	14/08/2000	13/08/1999
Applicant		
IMPRINT PHARMACEUTICALS LIMITED		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 4 sheets.

[X] It is also accompanied by a copy of each prior art document cited in this report.

1. **Basis of the report**

   a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

   [ ] the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

   b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing :

   [ ] contained in the international application in written form.

   [ ] filed together with the international application in computer readable form.

   [ ] furnished subsequently to this Authority in written form.

   [ ] furnished subsequently to this Authority in computer readble form.

   [ ] the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

   [ ] the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. [X] **Certain claims were found unsearchable** (See Box I).

3. [ ] **Unity of invention is lacking** (see Box II).

4. With regard to the **title**,

   [X] the text is approved as submitted by the applicant.

   [ ] the text has been established by this Authority to read as follows:

5. With regard to the **abstract**,

   [X] the text is approved as submitted by the applicant.

   [ ] the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is Figure No. 1

   [X] as suggested by the applicant.

   [ ] None of the figures.

   [ ] because the applicant failed to suggest a figure.

   [ ] because this figure better characterizes the invention.

INTERNATIONAL SEARCH REPORT

International Application No
P[redacted]B 00/03061

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 A61M5/20 A61M5/42 A61M5/46 A61M5/32

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 A61M

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P,X	WO 00 09184 A (IMPRINT PHARM LTD ;CROCKER PETER JOHN (GB)) 24 February 2000 (2000-02-24) the whole document	1-9, 11-14, 17-32, 36,37,40
X	FR 1 215 970 A (P. MUSSARD) 21 April 1960 (1960-04-21) the whole document	1,11,17, 18,36
X	CH 328 609 A (DUNMIRE RUSSELL P) 15 March 1958 (1958-03-15) page 5, line 81 -page 7, line 91; figures 7-11	1,19,20, 36

-/--

[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
13 October 2000	30/10/2000

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Jameson, P

Form PCT/ISA/210 (second sheet) (July 1992)

INTERNATIONAL SEARCH REPORT

International Application No
[redacted]GB 00/03061

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 92 20388 A (MEDIMECH INT LTD) 26 November 1992 (1992-11-26) abstract; figure 1 page 7, line 4 - line 33	1,19,20, 36
A	DE 34 05 671 A (SANDOZ AG) 22 August 1985 (1985-08-22) page 18, line 22 - line 29; figures 1-4	1,25-27
A	WO 95 29720 A (PA CONSULTING SERVICES ;REVELL WILLIAM JAMES (GB)) 9 November 1995 (1995-11-09) abstract; figure 1	1

Form PCT/ISA/210 (continuation of second sheet) (July 1992)

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Claims Nos.: 44

Claim 44 is written in a form which is contrary to PCT Rule 6.2(a).

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/GB 00/03061

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. [X] Claims Nos.: 45
because they relate to subject matter not required to be searched by this Authority, namely:

Rule 39.1(iv) PCT - Method for treatment of the human or animal body by therapy

2. [X] Claims Nos.: 44
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

Claim 44 is written in a form which is contrary to PCT Rule 6.2(a).

3. [ ] Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. [ ] As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. [ ] As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. [ ] As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. [ ] No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

[ ] The additional search fees were accompanied by the applicant's protest.

[ ] No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No
GB 00/03061

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 0009184 A	24-02-2000	AU 5431799 A	06-03-2000
FR 1215970 A	21-04-1960	NONE	
CH 328609 A	15-03-1958	NONE	
WO 9220383 A	26-11-1992	AU 1926792 A CA 2102920 A EP 0584207 A	30-12-1992 14-11-1992 02-03-1994
DE 3405671 A	22-08-1985	NONE	
WO 9529720 A	09-11-1995	AU 2313495 A	29-11-1995

PATENT COOPERATION TREATY

PTO

From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To:

COHEN, Alan Nicol
2 Grove Place
Tatsfield near Westerham
Kent TN16 2BB
GRANDE BRETAGNE

PCT

NOTIFICATION OF TRANSMITTAL OF THE INTERNATIONAL PRELIMINARY EXAMINATION REPORT
(PCT Rule 71.1)

Date of mailing *(day/month/year)*	21.11.2001
Applicant's or agent's file reference: 331	**IMPORTANT NOTIFICATION**

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/GB00/03061	14/08/2000	13/08/1999

Applicant
IMPRINT PHARMACEUTICALS LIMITED

1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary examination report and its annexes, if any, established on the international application.

2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.

3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices.

4. **REMINDER**

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices) (Article 39(1)) (see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary examination report. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide.

Name and mailing address of the IPEA/	Authorized officer
European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Wicha, M Tel.+49 89 2399-7281

Form PCT/IPEA/416 (July 1992)

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
331		
International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/GB00/03061	14/08/2000	13/08/1999
International Patent Classification (IPC) or national classification and IPC A61M5/20		
Applicant IMPRINT PHARMACEUTICALS LIMITED		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 8 sheets, including this cover sheet.

   ☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the report
   - II ☐ Priority
   - III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations suporting such statement
   - VI ☒ Certain documents cited
   - VII ☒ Certain defects in the international application
   - VIII ☒ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
06/03/2001	21.11.2001
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer Ceccarelli, D Telephone No. +49 89 2399 2653

Form PCT/IPEA/409 (cover sheet) (January 1994)

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/GB00/03061

I. Basis of the report

1. With regard to the **elements** of the international application *(Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17))*:
Description, pages:

1-12 as originally filed

Claims, No.:

1-34,36-45 as originally filed

Drawings, sheets:

1/2-2/2 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
- ☐ the claims, Nos.:

	No:	Claims	1,2,4,5,11,16,21,36,39
Inventive step (IS)	Yes:	Claims	9,10,12-15,17-20,40-43
	No:	Claims	1-8,11,16,21,22-34,36-43
Industrial applicability (IA)	Yes:	Claims	1-34,36-43
	No:	Claims	

2. Citations and explanations
see separate sheet

VI. Certain documents cited

1. Certain published documents (Rule 70.10)

and / or

2. Non-written disclosures (Rule 70.9)

see separate sheet

VII. Certain defects in the international application

The following defects in the form or contents of the international application have been noted:
see separate sheet

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:
see separate sheet

☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application.

☒ claims Nos. 44,45.

because:

☒ the said international application, or the said claims Nos. 45 relate to the following subject matter which does not require an international preliminary examination (*specify*):
see separate sheet

☒ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. 44 are so unclear that no meaningful opinion could be formed (*specify*):
see separate sheet

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☒ no international search report has been established for the said claims Nos. 44,45.

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

☐ the written form has not been furnished or does not comply with the standard.

☐ the computer readable form has not been furnished or does not comply with the standard.

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N) Yes: Claims 3,6-10,12-15,17-20,22-34,37,38,40-43

strike the needle assembly (items 11, 11' and 30 in figure 1) thereby inducing an acceleration of the needle to drive it into the surface (see second paragraph on page 7).

3. **Claims 2, 4, 5, 11, 16, 21, 36 and 39 are also not novel** (Article 33(2) PCT) in the light of the disclosure of document D1.
See for example page 7, second paragraph, third sentence, for the subject matter of claim 2, see stopping member 10 in figure 1 for the subject matter of claim 4, note that piston 30 is connected to needle 11 by the means of piston 10 (figure 1) - claim 5, see spring 9 in figure 1 - claim 11.
As for the subject matter of claim 16, the substance is indeed fed discontinuously to the needle, as it is fed during injection and not fed before and after it.
For the needle guide of claim 21 see item 18 in figure 1 and for the properties of the needle as defined in claim 39 note that they are common to all needles of hypodermic syringes.
As stated in section VIII below, claim 36 does not really define any technical feature with respect to the subject matter of claim 1.

4. **Claims 3, 6, 7, 8, 37 and 38 do not fulfil the requirements for inventive step** (Article 33(3) PCT), when the teaching of document D2 is taken in combination with that of the closest prior art document D1.
The use of a pneumatic system to cause a block to accelerate and perform an injection as well as the possibility of priming the injector again at the end of an injection by the means of the pneumatic system are known from document D2 (see abstract and lines 10-20 on page 13).
The skilled man would apply this arrangement when willing to enable the injection force to be varied according to the specific patient and when desiring to automate the use of the injector.
As for the rate of injections of claim 38 see also comments in section VIII below.

5. **Claims 22 to 34 do not seem to fulfil the requirements for inventive step** (Article 33(3) PCT) as they introduce dimensions which do not address any specific technical problem and therefore are considered as mere matter of design within the competence of the skilled man.

6. Claims 9, 10, 12-15, 17-20 and 40-43 seem to fulfil the requirements for novelty and inventive step (Article 33(2) and (3) PCT).
Their additional features are not disclosed in the available prior art documents and seem to allow a better control of several aspects of the injection procedure.

Re Item VI

Certain documents cited

Certain published documents (Rule 70.10)

Application No Patent No	Publication date *(day/month/year)*	Filing date *(day/month/year)*	Priority date *(valid claim)* *(day/month/year)*
WO 00 09184 A	24 February 2000	13 August 1999	13 August 1998

The applicant's attention is drawn to the fact that this document would deprive most of the claims on file of novelty.

Re Item VII

Certain defects in the international application

1. Document D1 should have been cited in the description, since it represents the closest state of the art in the field of the application (Rule 5.1(a)(ii) PCT).

2. The claims do not contain any reference signs to the figures, which would be appropriate to facilitate the understanding of the claims themselves (Rule 6.2(b) PCT).

3. The independent claim is not drafted in the two-part form, as normally required by Rule 6.3(b) PCT.

Re Item VIII

Certain observations on the international application

1. Claim 19 does not meet the requirements of Article 6 PCT, as it is not clear for which subject matter protection is sought.
   In particular the position of the "connection means", which are "between and the syringe" is not defined.

2. In claims 36 and 38 method steps rather than technical features of an apparatus are defined. They are not assumed to delimit the scope of protection (see also Rule 6.3(a) PCT).

3. The dependency of claims 6, 10 and 20 is not clear (Article 6 PCT).
   In particular a claim cannot depend on itself (claims 6 and 10) and the syringe to which in claim 20 it is referred to was not defined in claim 16.

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PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
331		
International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/GB00/03061	14/08/2000	13/08/1999

International Patent Classification (IPC) or national classification and IPC
A61M5/20

Applicant
IMPRINT PHARMACEUTICALS LIMITED

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 8 sheets, including this cover sheet.

   ☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the report
   - II ☐ Priority
   - III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations suporting such statement
   - VI ☒ Certain documents cited
   - VII ☒ Certain defects in the international application
   - VIII ☒ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
06/03/2001	21.11.2001
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer Ceccarelli, D Telephone No. +49 89 2399 2653

Form PCT/IPEA/409 (cover sheet) (January 1994)

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/GB00/03061

I. Basis of the report

1. With regard to the **elements** of the international application *(Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17))*:
Description, pages:

1-12 as originally filed

Claims, No.:

1-34,36-45 as originally filed

Drawings, sheets:

1/2-2/2 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer-readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
- ☐ the claims, Nos.:

☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application.

☒ claims Nos. 44,45.

because:

☒ the said international application, or the said claims Nos. 45 relate to the following subject matter which does not require an international preliminary examination (*specify*):
see separate sheet

☒ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. 44 are so unclear that no meaningful opinion could be formed (*specify*):
see separate sheet

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☒ no international search report has been established for the said claims Nos. 44,45.

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

☐ the written form has not been furnished or does not comply with the standard.

☐ the computer readable form has not been furnished or does not comply with the standard.

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N) Yes: Claims 3,6-10,12-15,17-20,22-34,37,38,40-43

	No:	Claims	1,2,4,5,11,16,21,36,39
Inventive step (IS)	Yes:	Claims	9,10,12-15,17-20,40-43
	No:	Claims	1-8,11,16,21,22-34,36-43
Industrial applicability (IA)	Yes:	Claims	1-34,36-43
	No:	Claims	

2. Citations and explanations
see separate sheet

VI. Certain documents cited

1. Certain published documents (Rule 70.10)

and / or

2. Non-written disclosures (Rule 70.9)

see separate sheet

VII. Certain defects in the international application

The following defects in the form or contents of the international application have been noted:
see separate sheet

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:
see separate sheet

Re Item III

Non-establishment of Report with regard to novelty, inventive step and industrial applicability

No examination according to Article 33(1) PCT has been carried out for claim 45, as it defines methods for treating the human or animal body (Rule 67.1(iv) PCT).
No examination according to Article 33(1) PCT has been carried out for claim 44, as it is not clear for which subject matter protection is sought (Article 6 PCT).
The reference to the drawings is against Rule 6.2(a) PCT and in this case makes it impossible to clearly delimit the scope of protection.
Moreover no meaningful examination could have anyway been carried out for said claims 44 and 45, since no Search Report has been established for them (Rule 66.1(e) PCT).

Re Item V

Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Reference is made to the following documents:

   D1: WO 92 20388 A (MEDIMECH INT LTD) 26 November 1992 (1992-11-26)
   D2: DE 34 05 671 A (SANDOZ AG) 22 August 1985 (1985-08-22)

2. **The subject matter of claim 1 does not meet the requirements for novelty** (Article 33(2) PCT) as it is anticipated by the disclosure of document D1, considered to represent the closest prior art for the present application.
   Said document D1 shows an apparatus for injecting a substance into a surface which apparatus comprises a needle (item 11 in figure 1), a container for the substance to be injected (item 19 in figure 1), a means for applying the substance from the container to the tip of the needle (slot 32 in figure 1 and open rear end of needle 11 in figure 1), a means for driving the needle (items 27, 10 and 11' in figure 1) to penetrate the surface and deliver the substance thereto which means comprises a block (item 5 in figure 1, in particular its end 20) slidably mounted in a conduit (item 24 in figure 1) which block is accelerated by a controlled force to

strike the needle assembly (items 11, 11' and 30 in figure 1) thereby inducing an acceleration of the needle to drive it into the surface (see second paragraph on page 7).

3. **Claims 2, 4, 5, 11, 16, 21, 36 and 39 are also not novel** (Article 33(2) PCT) in the light of the disclosure of document D1.
See for example page 7, second paragraph, third sentence, for the subject matter of claim 2, see stopping member 10 in figure 1 for the subject matter of claim 4, note that piston 30 is connected to needle 11 by the means of piston 10 (figure 1) - claim 5, see spring 9 in figure 1 - claim 11.
As for the subject matter of claim 16, the substance is indeed fed discontinuously to the needle, as it is fed during injection and not fed before and after it.
For the needle guide of claim 21 see item 18 in figure 1 and for the properties of the needle as defined in claim 39 note that they are common to all needles of hypodermic syringes.
As stated in section VIII below, claim 36 does not really define any technical feature with respect to the subject matter of claim 1.

4. **Claims 3, 6, 7, 8, 37 and 38 do not fulfil the requirements for inventive step** (Article 33(3) PCT), when the teaching of document D2 is taken in combination with that of the closest prior art document D1.
The use of a pneumatic system to cause a block to accelerate and perform an injection as well as the possibility of priming the injector again at the end of an injection by the means of the pneumatic system are known from document D2 (see abstract and lines 10-20 on page 13).
The skilled man would apply this arrangement when willing to enable the injection force to be varied according to the specific patient and when desiring to automate the use of the injector.
As for the rate of injections of claim 38 see also comments in section VIII below.

5. **Claims 22 to 34 do not seem to fulfil the requirements for inventive step** (Article 33(3) PCT) as they introduce dimensions which do not address any specific technical problem and therefore are considered as mere matter of design within the competence of the skilled man.

6. Claims 9, 10, 12-15, 17-20 and 40-43 seem to fulfil the requirements for novelty and inventive step (Article 33(2) and (3) PCT).
Their additional features are not disclosed in the available prior art documents and seem to allow a better control of several aspects of the injection procedure.

Re Item VI
Certain documents cited

Certain published documents (Rule 70.10)

Application No Patent No	Publication date *(day/month/year)*	Filing date *(day/month/year)*	Priority date *(valid claim)* *(day/month/year)*
WO 00 09184 A	24 February 2000	13 August 1999	13 August 1998

The applicant's attention is drawn to the fact that this document would deprive most of the claims on file of novelty.

Re Item VII
Certain defects in the international application

1. Document D1 should have been cited in the description, since it represents the closest state of the art in the field of the application (Rule 5.1(a)(ii) PCT).

2. The claims do not contain any reference signs to the figures, which would be appropriate to facilitate the understanding of the claims themselves (Rule 6.2(b) PCT).

3. The independent claim is not drafted in the two-part form, as normally required by Rule 6.3(b) PCT.

Re Item VIII
Certain observations on the international application

1. Claim 19 does not meet the requirements of Article 6 PCT, as it is not clear for which subject matter protection is sought.
   In particular the position of the "connection means", which are "between and the syringe" is not defined.

2. In claims 36 and 38 method steps rather than technical features of an apparatus are defined. They are not assumed to delimit the scope of protection (see also Rule 6.3(a) PCT).

3. The dependency of claims 6, 10 and 20 is not clear (Article 6 PCT).
   In particular a claim cannot depend on itself (claims 6 and 10) and the syringe to which in claim 20 it is referred to was not defined in claim 16.

PATENT COOPERATION TREATY

From the:
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To:
COHEN, Alan Nicol
2 Grove Place
Tatsfield near Westerham
Kent TN16 2BB
GRANDE BRETAGNE

PCT

WRITTEN OPINION

(PCT Rule 66)

Date of mailing *(day/month/year)*	23.07.2001
Applicant's or agent's file reference: 331	**REPLY DUE** **within 3 month(s)** from the above date of mailing

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/GB00/03061	14/08/2000	13/08/1999

International Patent Classification (IPC) or both national classification and IPC
A61M5/20

Applicant
IMPRINT PHARMACEUTICALS LIMITED

1. This written opinion is the **first** drawn up by this International Preliminary Examining Authority.

2. This opinion contains indications relating to the following items:

I	☒	Basis of the opinion
II	☐	Priority
III	☒	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
IV	☐	Lack of unity of invention
V	☒	Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
VI	☒	Certain document cited
VII	☒	Certain defects in the international application
VIII	☒	Certain observations on the international application

3. The applicant is hereby **invited to reply** to this opinion.

When? See the time limit indicated above. The applicant may, before the expiration of that time limit, request this Authority to grant an extension, see Rule 66.2(d).

How? By submitting a written reply, accompanied, where appropriate, by amendments, according to Rule 66.3. For the form and the language of the amendments, see Rules 66.8 and 66.9.

Also: For an additional opportunity to submit amendments, see Rule 66.4. For the examiner's obligation to consider amendments and/or arguments, see Rule 66.4 bis. For an informal communication with the examiner, see Rule 66.6.

If no reply is filed, the international preliminary examination report will be established on the basis of this opinion.

4. The final date by which the international preliminary examination report must be established according to Rule 69.2 is: 13/12/2001.

Name and mailing address of the international preliminary examining authority:
European Patent Office
D-80298 Munich
Tel. +49 89 2399 - 0 Tx: 523656 epmu d
Fax: +49 89 2399 - 4465

Authorized officer / Examiner
Ceccarelli, D

Formalities officer (incl. extension of time limits)
Ertl, L
Telephone No. +49 89 2399 7447

I. Basis of the opinion

1. With regard to the **elements** of the international application (Replacement *sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this opinion as "originally filed"*):

Description, pages:

1-12 as originally filed

Claims, No.:

1-34,36-45 as originally filed

Drawings, sheets:

1/2-2/2 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
- ☐ the claims, Nos.:

☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been and will not be examined in respect of:

☐ the entire international application,

☒ claims Nos. 44,45,

because:

☒ the said international application, or the said claims Nos. 45 relate to the following subject matter which does not require an international preliminary examination (*specify*):
see separate sheet

☒ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. 44 are so unclear that no meaningful opinion could be formed (*specify*):
see separate sheet

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☒ no international search report has been established for the said claims Nos. 44,45.

2. A written opinion cannot be drawn due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

☐ the written form has not been furnished or does not comply with the standard.

☐ the computer readable form has not been furnished or does not comply with the standard.

V. Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims	1,2,4,5,11,16,21,36,39
Inventive step (IS)	Claims	3,7,8,22-34,37,38

Industrial applicability (IA) Claims

2. Citations and explanations
see separate sheet

VI. Certain documents cited

1. Certain published documents (Rule 70.10)

and / or

2. Non-written disclosures (Rule 70.9)

see separate sheet

VII. Certain defects in the international application

The following defects in the form or contents of the international application have been noted:
see separate sheet

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:
see separate sheet

Re Item III

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

No examination according to Article 33(1) PCT will be carried out for claim 45, as it defines methods for treating the human or animal body (Rule 67.1(iv) PCT).
No examination according to Article 33(1) PCT will be carried out for claim 44, as it is not clear for which subject matter protection is sought (Article 6 PCT).
The reference to the drawings is against Rule 6.2(a) PCT and makes it impossible to clearly delimit the scope of protection.
Moreover no examination will anyway be carried out for said claims 44 and 45, since no Search Report has been established for them (Rule 66.1(e) PCT).

Re Item V

Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Reference is made to the following documents:

   D1: WO 92 20388 A (MEDIMECH INT LTD) 26 November 1992 (1992-11-26)
   D2: DE 34 05 671 A (SANDOZ AG) 22 August 1985 (1985-08-22)

2. The subject matter of claim 1 does not meet the requirements for novelty (Article 33(2) PCT) as it is anticipated by the disclosure of document D1, considered to represent the closest prior art for the present application.
   Said document D1 shows an apparatus for injecting a substance into a surface which apparatus comprises a needle (item 11 in figure 1), a container for the substance to be injected (item 19 in figure 1), a means for applying the substance from the container to the tip of the needle (slot 32 in figure 1 and open rear end of needle 11 in figure 1), a means for driving the needle (items 27, 10 and 11' in figure 1) to penetrate the surface and deliver the substance thereto which means comprises a block (item 5 in figure 1, in particular its end 20) slidably mounted in a conduit (item 24 in figure 1) which block is accelerated by a controlled force to strike the needle assembly (items 11, 11' and 30 in figure 1) thereby inducing an

acceleration of the needle to drive it into the surface (see second paragraph on page 7).

3. Claims 2, 4, 5, 11, 16, 21, 36 and 39 are also not novel (Article 33(2) PCT) in the light of the disclosure of document D1.
See for example page 7, second paragraph, third sentence, for the subject matter of claim 2, see stopping member 10 in figure 1 for the subject matter of claim 4, note that piston 30 is connected to needle 11 by the means of piston 10 (figure 1) - claim 5, see spring 9 in figure 1 - claim 11.
As for the subject matter of claim 16, the substance is indeed fed discontinuously to the needle, as it is fed during injection and not fed before and after it.
For the needle guide of claim 21 see item 18 in figure 1 and for the properties of the needle as defined in claim 39 note that they are common to all needles of hypodermic syringes.
As stated in section VIII below, claim 36 does not really define any technical feature with respect to the subject matter of claim 1.

4. Claims 3, 7, 8, 37 and 38 do not fulfil the requirements for inventive step (Article 33(3) PCT), when the teaching of document D2 is taken in combination with that of the closest prior art document D1.
The use of a pneumatic system to cause a block to accelerate and perform an injection as well as the possibility of priming the injector again at the end of an injection by the means of the pneumatic system are known from document D2 (see abstract and lines 10-20 on page 13).
The skilled man would apply this arrangement when willing to enable the injection force to be varied according to the specific patient and when desiring to automate the use of the injector.
As for the rate of injections of claim 38 see also comments in section VIII below.

5. Claims 22 to 34 do not seem to fulfil the requirements for inventive step (Article 33(3) PCT) as they introduce dimensions which do not address any specific technical problem and therefore are considered as mere matter of design within the competence of the skilled man.

Re Item VI
Certain documents cited

Certain published documents (Rule 70.10)

Application No Patent No	Publication date *(day/month/year)*	Filing date *(day/month/year)*	Priority date *(valid claim)* *(day/month/year)*
WO 00 09184 A	24 February 2000	13 August 1999	13 August 1998

The applicant's attention is drawn to the fact that this document would deprive most of the claims on file of novelty.

Re Item VII
Certain defects in the international application

1. Document D1 should be cited in the description, since it represents the closest state of the art in the field of the application (Rule 5.1(a)(ii) PCT).

2. The claims do not contain any reference signs to the figures, which would be appropriate to facilitate the understanding of the claims themselves (Rule 6.2(b) PCT).

3. The independent claim is not drafted in the two-part form, as normally required by Rule 6.3(b) PCT.

Re Item VIII
Certain observations on the international application

1. Claim 19 does not meet the requirements of Article 6 PCT, as it is not clear for which subject matter protection is sought.
   In particular the position of the "connection means", which are "between and the syringe" is not defined.

2. In claims 36 and 38 method steps rather than technical features of an apparatus

are defined. They are not assumed to delimit the scope of protection (see also Rule 6.3(a) PCT).

3. The dependency of claims 10 and 20 is not clear (Article 6 PCT).
In particular a claim cannot depend on itself (claim 10) and the syringe to which in claim 20 it is referred to was not defined in claim 16.

4. The applicant is invited to file new claims which take into account the above comments and Article 33.2(b) PCT.